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Document ID: WO 9834118 A1 1.

Entry 1 of 5

File: EPAB

Aug 6, 1998

PUB-NO: WO009834118A1

DOCUMENT-IDENTIFIER: WO 9834118 A1

TITLE: DIAGNOSTIC METHODS AND COMPOSITIONS BASED ON THE DISTRIBUTION OF RAD51

PUBN-DATE: August 6, 1998

INVENTOR-INFORMATION:

COUNTRY NAME N/AHAFF, THOMAS N/ARADDING, CHARLES N/AREDDY, GURU  $A \setminus N$ 

WARD, DAVID

INT-CL (IPC):  $\underline{G01}$   $\underline{N}$   $\underline{33/574}$ ;  $\underline{G01}$   $\underline{N}$   $\underline{33/50}$ ;  $\underline{C07}$   $\underline{K}$   $\underline{14/47}$   $\underline{FUR-CL}$  (EPC):  $\underline{G01N033/50}$ ;  $\underline{G01N033/574}$ ,  $\underline{G01N033/574}$ ,  $\underline{G01N033/574}$ 

ABSTRACT:

Method of diagnosing individual at risk for a disease comprising determining the distribution of RAD51 foci in a tissue type of a first individual; and comparing said distribution of RAD51 foci form a second normal tissue type from said first individual or a second unaffected individual.

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Document ID: AU 9860512 A, WO 9834118 A1 2.

Entry 2 of 5

File: DWPI

Aug 25, 199

DERWENT-ACC-NO: 1998-437609

DERWENT-WEEK: 199903

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TITLE: Diagnosing cancer and apoptotic disease from distribution of Rad51 foci

in cells - also detecting cells with mutant Rad51 genes, screening for agents

that bind Rad51 and inducing apoptosis by increasing Rad51 activity

INVENTOR-NAME: HAFF, T; RADDING, C; REDDY, G; WARD, D; GURUWARD, D

; RADDING, T ; REDDY, C

PRIORITY-DATA: 1998US-0045668 (January 14, 1998) , 1997US-0035834 (January 30,

1997) , 1997US-0045668 (May 6, 1997)

PATENT-FAMILY:

PUB-DATE PUB-NO August 25, 1998 AU 9860512 A

August 6, 1998

LANGUAGE N/A

PAGES 000

MAIN-IPC G01N 033/57

WO 9834118 A1

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G01N 033/57

INT-CL (IPC):  $C07 \times 14/47$ ;  $G01 \times 33/50$ ;  $G01 \times 33/574$ 

ABSTRACTED-PUB-NO: WO 9834118A

BASIC-ABSTRACT: Individuals at risk of disease are identified by: (i) determining the distribution of Rad51 foci (A) in a selected tissue type; and (ii) comparing this with the distribution in either normal tissue from the same subject or from a second, unaffected subject, any difference indicating risk of disease associated with aberrant loci.

Also new are: (1) identifying apoptotic or stressed cells from aberrant distribution of (A); (2) identifying cells containing a mutant Rad51 gene by comparing all or part of the gene sequence with that of an endogenous Rad51 gene; (3) a method similar to (2) for determining Rad51 genotype; (4) a method of screening for agents (B) able to bind Rad51 or to alter its activity; (5) a method for inducing apoptosis by increasing Rad51 activity; (6) a composition containing nucleic acids encoding Rad51 and a tumour suppressor; and (7) a composition containing recombinant Rad51 and tumour suppressor proteins.

USE - The method is used to identify patients with, or at risk of developing, cancer (lymphoma, leukaemia or many forms of solid cancer, particularly of breast, skin, brain, colon and prostate), apoptotic disease (e.g. acquired immune deficiency syndrome, liver failure, neurodegeneration, multiple sclerosis, aplastic anaemia, diabetes mellitus etc.) or diseases associated with cellular stresses (e.g. cardiovascular disease, immune system decline etc.), and the extent of aberrant distribution is correlated with severity. Method (1) is particularly applied to cells with oxidative, hypoxic, cold or heat stress. Methods (2) and (3) are used to diagnose disease or susceptibility and method (5) for treatment of cancer cells. (B) are potential therapeutic agents.

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## Document ID: AU 9852439 A, WO 9820030 A2 3.

Entry 3 of 5

File: DWPI

May 29, 199

DERWENT-ACC-NO: 1998-286860

DERWENT-WEEK: 199841

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TITLE: New compounds that bind to and inactivate mammalian Rad51 protein used to inhibit cell proliferation or to induce cell death, e.g. in treatment

of cancer or auto-immune disease

INVENTOR-NAME: HASTY, P

PRIORITY-DATA: 1996US-0758280 (November 5, 1996)

PATENT-FAMILY:

MAIN-IPC PAGES LANGUAGE PUB-DATE PUB-NO C07K 014/00 000 May 29, 1998  $A \setminus N$ AU 9852439 A C07K 014/00 054 May 14, 1998 Ε WO 9820030 A2

INT-CL (IPC): C07 K 14/00; C07 K 14/435; C12 P 21/02; C12 Q 1/25

ABSTRACTED-PUB-NO: WO 9820030A

BASIC-ABSTRACT: Compounds (I) that bind intracellularly to, and inactivate, mammalian Rad51 are new. Also new are: (1) truncated Rad51 protein encoded by rad51TR1-131; (2) altered Rad51 protein encoded by rad51K-A134; (3) method for screening compounds (II) that disrupt mammalian double-stra nded break (DSB) repair by detecting microsatellites and chromosome loss in cells and disruption of strand exchange in vitro, and (4) yeast 2-hybrid system and biological binding assays for identifying compounds (III) that disrupt function of Rad51 and Rad52.

USE - Engineered Rad51, (II) and (III) are used to inhibit cell proliferation or to induce cell death, particularly for treatment of proliferative disorders, e.g. autoimmune diseases (e.g. arthritis or inflammatory bowel disease), all types of cancer, inflammation, graft rejection, or proliferation following angioplasty or surgery. Rad51 function is essential for cell proliferation and/or viability (probably it is involved in DBS repair). Rad51 polypeptides are also used to raise specific antibodies (Ab). These are used to detect/quan tify the proteins, e.g. for diagnosis, monitoring and prognosis of treatments with agents that inhibit DBS repair, as therapeutic inhibitors and for affinity purification. (I) are administered by injection or inhalation, topically, from sustained-release formulations, and optionally also expressed from gene therapy vectors.

## Citation Front Review Classification Date Reference Claims

Document ID: JP 07143890 A

Entry 4 of 5

File: DWPI

Jun 6, 1995

DERWENT-ACC-NO: 1995-236467

DERWENT-WEEK: 199531

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TITLE: Structural gene encoding RAD51, used in production of RAD51 - used to study drugs against diseases caused by DNA damage, e.g. by UV or X radiation,

and to improve efficiency if gene therapy targetting

INVENTOR-NAME:

PRIORITY-DATA: 1993JP-0127594 (May 28, 1993)

PATENT-FAMILY:

MAIN-IPC PAGES LANGUAGE PUB-DATE PUB-NO C12N 015/12019 N/AJune 6, 1995 JP 07143890 A

INT-CL (IPC): C12 N 1/19; C12 N 5/10; C12 N 15/12; C12 P 21/02; C12 N 1/19; C12 R 1/19865;  $\overline{\text{C12}}$   $\underline{\text{P}}$   $\underline{21/02}$ ;  $\overline{\text{C12}}$   $\underline{\text{R}}$   $\underline{1/865}$ ;  $\underline{\text{C12}}$   $\underline{\text{P}}$   $\underline{21/02}$ ;  $\underline{\text{C12}}$   $\underline{\text{R}}$   $\underline{1/19}$ ;  $\underline{\text{C12}}$   $\underline{\text{P}}$   $\underline{21/02}$ ; C12 R 1/91

ABSTRACTED-PUB-NO: JP07143890A

BASIC-ABSTRACT: A structural gene RAD51 encoding the amino acid sequences of 339, 365 or 339 residues given in the specification, is new. Also claimed are: (1) a recombinant vector contg. the RAD51 gene; (2) transformants, e.g. E. coli, yeast or mammal cell, containing the vector of (1); (3) the process for producing Rad51; and (4) a DNA encoding an amino acid sequence which has 60% or more homology with that of Rad51.

USE - The human  $\frac{RAD51}{}$  gene is concerned with specific genetic recombination in the meiotic phase, site-specific recombination in the rearrangement of antibody genes or repair of mismatched base pair. The RAD51 gene may be used in research of drugs effective for <u>diseases</u>, caused by DNA damage (e.g. by X-ray or UV) or in safety tests of drugs.

ADVANTAGE - The RAD51 protein is effective in increasing the efficacy of gene targeting in gene therapy.

## Title Citation Front Review Classification Date Reference Claims KWC Image

Document ID: JP 06141863 A 5.

Entry 5 of 5

File: DWPI

May 24, 199

DERWENT-ACC-NO: 1994-205025

DERWENT-WEEK: 199425

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TITLE: Mouse gene participating in homologous recombination reaction - useful

for improving the frequency of homologous recombination in gene therapy

INVENTOR-NAME:

PRIORITY-DATA: 1992JP-0299714 (November 10, 1992)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

JP 06141863 A

May 24, 1994

A/N

800

C12N 015/12

INT-CL (IPC): C12N 1/19; C12N 15/12; C12Q 1/68

ABSTRACTED-PUB-NO: JP06141863A

BASIC-ABSTRACT: Mouse genes participating in homologous recombination reaction,

partic. homologous to yeast Rad51 and E. coli recA sequence are new.

Also claimed are 2 particular gene sequences.

Pref. rad51 and recA sequences are isolated from mouse and identified with those of synthetic sequences by conventional methods.

USE - Isolated yeast Rad51 and E. coli genes improve the frequency of homologous recombination for gene therapy and the prepn. of disease model animals.

In an example, RNA from mouse testicle was isolated and cDNA was prepd. using a reverse transcription enzyme. PCR of the cDNA provided 2 oligonucleotide primers. Their base seudences were determined. In E. coli Le392, a phage of mouse cDNA library was seeded, cultured and hybridised using a probe of 358 bp labelled with alpha-32P-dCTP to give clone pMR51. A rad cDNA isolated from a variant yeast Rad51 X3672-3c (a rad 51-1, ura3 leu2 trp1 his4 lys2 ade2) was ligated down stream of a galactose promoter of shuttle vector pYES and transformed. Colony formation of yeast Rad51 gene as a positive control and mouse Rad cDNA as a negative control were introduced into yeast X3672-3c and their homogenous recombinant mechanism as with those of eucaryote species including humans was confirmed.

		02-13-5	Cross	Ravism	Classification	Date	Reference	Claims	KWAC	Image
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Term	Documents
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